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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,101	05/18/2001	Robert D. Mass	3118/IH146US1	9233

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EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/31/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/863,101

Applicant(s)

MASS, ROBERT D.

Examiner

MISOOK YU, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 21-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4, 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

Applicant's election without traverse of group III claims 21-23 in Paper No. 10 is acknowledged.

Claims 21-23 are pending and examined on merits.

***Claim Objections***

Claim 22 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 22 depends from claim 21 drawn to method of detecting gene amplification, not detecting protein production.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: correlating step linking any detection result to the purpose stated in the preamble stated in claim 21.

Claim 21 is confusing therefore indefinite because the claim is not clear whether an increased erbB gene amplification or a decreased erbB gene gene amplification is indicative of a patient disposed to respond favorably to an ErbB antagonist. For the purpose of this office action, this examiner will assume, based on the specification at Examples 1 and 2, that detection of Her2 gene amplification in a cancer patient is

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indicative of favorable response to Herceptin (an ErbB antagonist). However, this treatment does not relieve applicant the burden of responding to this rejection.

~~Claim 22 depends from claim 21 drawn to detection of a gene amplification~~  
method and the specification at page 7 lines 16-21 defines gene amplification as increased transcription, not increased protein translation or protein concentration and claim 22 recites the limitation "immunohistochemistry" in line 2. immunohistochemistry detects protein, not gene amplification, therefore it appears that there is insufficient antecedent basis for claim 22.

Claim 22 recites the limitation "the subject" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 22 recites "a 0 or 1+" but it is not clear what the metes and bounds are for the limitation.

Claim 22 is confusing because it is not clear how a 0 or 1+ score by immunohistochemistry on a formaldehyde-fixed tissue sample is related to the purpose stated in the preamble of claim 21 or to claim 21.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being **enabling for Her2 gene amplification and Herceptin**, does not reasonably provide enablement for **any other erbB gene amplification and any other ErbB antagonist**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claim is interpreted as drawn to method of detecting an erbB gene amplification for screening cancer patients for prediction of favorable response to an ErbB antagonist. The specification at Examples 1 and 2 (pages 27-33) teaches method of Her2 detection using FISH analysis and also teaches that Her2-positive patients responds favorably to Herceptin alone or combined with

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other chemotherapeutic agents. However, the specification does not teach any correlation between detection of any other erbB gene amplification in a cancer patient to any other ErbB-antagonist. Ross et al (IDS-5, 1998, Stem Cell, vol. 16, pages 413-428) teach considerations necessary in bringing a cancer biomarker to successful clinical application. Ross et al teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials and this validation process requires a large number of clinical samples and also requires recruiting a large number of patients for clinical trials (see the entire article, especially abstract, Tables 2-7). Ross et al teaches at Table 1 that erbB gene encompasses at least four different genes. The reference further teaches that the potential value of gene amplification status for the prediction of response to cancer therapy requires a large number of clinical samples. See the entire article. The essential element in the validation of an marker for prediction of cancer treatment outcome is the ability to test the marker on clinical material obtained from subjects with comparison to patient's response to a given cancer treatment. This irrefutable link between an antecedent marker and subsequent acknowledged treatment outcome is the essence of a valid intermediate end point marker. Clearly, prior to the successful application of newly described markers for treatment protocol, markers must be validated against treatment and the marker predictive value must be confirmed in prospective population trials. See Table 2, 4-7.

The specification does not teach any correlation between any other ErbB gene amplification other than her2 to any other ErbB antagonist other than anti-her2. Considering the unpredictability of using an untested marker for predicting cancer treatment outcome, limited guidance in the specification, lack of working examples, it is concluded that undue experimentation is necessary to practice the full scope of the instant invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless —

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by either Ross et al (#5 of IDS filed 7-26-2002, 1998, Stem Cell, vol. 16, pages 413-428) or Ross et al (#209 of IDS filed 2-7-2002, 1997, Cancer, vol., 79, pages 2162-2170).

Claims 21-23 are interpreted as drawn to method of detecting Her2 gene amplification for screening cancer patients for prediction of favorable response to an anti-her2 antibody.

Ross et al (#5 of IDS filed 7-26-2002, 1998, Stem Cell, vol. 16, pages 413-428) teach method of detection Her2, and Her2 status for potential value for predicting response to anti-cancer therapy, and further teach that anti-Her2 therapy alone or in combination with other anti-cancer therapy has favorable treatment outcome in patients with Her-2 gene amplification or Her-2 protein over-expression. See the entire article, especially abstract, Table 2-9, and Figs. 1 and 2.

Ross et al (#209 of IDS filed 2-7-2002, 1997, Cancer, vol., 79, pages 2162-2170) teach method of detecting Her2 gene amplification using FISH analysis or immunohistochemistry and further teach use of status of Her2 gene expression for a prognostic marker in anti-cancer therapy. See entire article, especially abstract, Materials and Methods section, and the last paragraph of the article.

Thus, either Ross et al (#5 of IDS filed 7-26-2002, 1998, Stem Cell, vol. 16, pages 413-428) or Ross et al (#209 of IDS filed 2-7-2002, 1997, Cancer, vol., 79, pages 2162-2170) anticipates the instant claims.

### **Conclusion**

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-

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308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

— If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu  
December 18, 2002

*Mary Mosher*  
**MARY E. MOSHER**  
**PRIMARY EXAMINER**  
**GROUP 1800**  
1600